

ABSTRACT

The invention provides chimeric proteins having at least two functional protein units, each containing the dimerization domain of a member of the steroid/thyroid hormone nuclear receptor superfamily. The chimeric proteins can fold under crystallization conditions to form functional entities. The functional entities optionally contain a novel flexible peptide linker of variable lengths between at least two of the protein units. In a preferred embodiment, the linker is designed to be increased in increments of 12 amino acids each to aid in preparation of variant chimeric proteins. The DNA binding characteristics of the invention functional entities differ from those of wild-type complexes formed between "monomeric" receptors and their binding partners. Some functional entities, e.g. dimers expressed as fusion proteins, transactivate responsive promoters in a manner similar to wild-type complexes, while others do not promote transactivation and function instead essentially as constitutive repressors. The invention further provides nucleotide sequences encoding the invention chimeric proteins, cells containing such nucleotide sequences, and methods for using the invention chimeric proteins to modulate expression of one or more exogenous genes in a subject organism. In addition, isolated protein crystals suitable for x-ray diffraction analysis and methods for obtaining putative ligands for the invention chimeric proteins are provided.